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Lung cancer risk and red meat consumption among Iowa women

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Abstract

Objective: Some epidemiologic studies suggest that diets high in total fat, saturated fat, or cholesterol are associated with increased risk of lung cancer. Others suggest that diets high in red meat consumption, particularly well-done red meat, are a lung cancer risk factor. In Iowa, we had the opportunity to investigate concurrently the role of meat intake and macronutrients in lung cancer etiology. *Methods*: A population-based case-control study of both non-smoking and smoking women was conducted in Iowa. A 70-item food frequency questionnaire (FFQ) was completed by 360 cases and 574 frequency-matched controls. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using logistic regression. Multivariate models included age, education, pack–years of smoking, yellow–green vegetable intake, fruit/fruit juice intake, nutrient density calories, previous non-malignant lung disease, alcohol consumption and body mass index (BMI). *Results:* When comparing the fifth (highest) to the first (lowest) quintile of consumption of total fat, saturated fat and cholesterol, we obtained odds ratios of 2.0 (1.3–3.1), 3.0 (1.9–4.7), and 2.0 (1.3–3.0) respectively. However, when red meat was entered into the model along with total fat, saturated fat or cholesterol, the excess risk for the macronutrients disappeared while an odds ratio of 3.3 (1.7–7.6) was obtained for red meat. The odds ratios for red meat consumption were similar among adenocarcinoma cases, OR = 3.0 (1.1–7.9) and non–adenocarcinoma cases, OR = 3.2 (1.3–8.3) and among life-time nonsmokers and ex-smokers OR = 2.8 (1.4–5.4), and current smokers, OR = 4.9 (1.1–22.3). Yellow–green vegetables were protective with an odds ratio of 0.4 (0.2–0.7). *Conclusions:* Consumption of red meat, was associated with an increased risk of lung cancer even after controlling for total fat, saturated fat, cholesterol, fruit, yellow–green vegetable consumption and smoking history, while yellow–green vegetables are associated with a decreased risk of lung cancer.

Keywords: Lung cancer; Red meat; Case-control; Iowa women; Diet

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1. Background

Several epidemiologic studies suggest that lung cancer risk may be associated with intake of cholesterol, total and saturated fat [1–6]; others investigated the role of meat intake [7–10]. In a Swedish study, lung cancer risk was not associated with consumption of meat or fish [7]. In contrast, a study from Uruguay found increased risk with higher consumption of fried meat [8] and in a cohort study of 20 195 United States' participants in the 1987 National Health Interview Survey found red meat to be positively associated with lung cancer mortality [9]. Consumption of well-done, well-browned meat has been associated with increased risk of lung cancer [10] and cancers of various other sites [11–15]. Well-done meat has been assumed to be a surrogate of exposure to heterocyclic amines, but evidence of carcinogenicity of these compounds in humans is not conclusive. In a population-based case-control study of lung cancer among Iowa women designed to assess the role of residential radon and other potential risk factors, we obtained detailed information on diet from a 70-item food-frequency questionnaire.

2. Methods

2.1. Case participants

Cases were identified through the Iowa Cancer Registry, which has been a part of the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute since its inception in 1973. Once a case was identified, a letter was sent to the patient's physician requesting permission to contact the patient. When approval was received from the physician, a telephone call was made to determine the study subject's eligibility and willingness to participate after informed consent was established. A questionnaire was mailed to the participant (or proxy) with instructions to complete the instrument before the study technician made the home visit. Appointments were made for the field technician's home visit. During the home visit, questionnaires were reviewed with the respondent to assess completeness and to help the respondent answer questions that confused them. The completion of incomplete questions or sections was faciliated by face-to-face interviews. Proxy interviews were with the lung cancer patient's next-of-kin. Usually the next-of-kin was an adult daughter, sometimes in was a neighbor who assisted in food preparation prior to onset of disease. As part of the residential radon study, radon dosimeters were then placed within the home.

The case series included 431 newly diagnosed female cases between the age of 40–84 years who were Iowa residents at the time of diagnosis with primary invasive (not in situ) lung carcinoma diagnosed between May 1, 1993 and October 30, 1996, without any prior primary invasive lung carcinoma. Since the study was designed to assess the effect of residential radon on the risk of lung cancer, study participants also had to occupy their current home for twenty years or more [16]. To obtain a reliable histologic diagnosis, pathologic materials were retrieved for 423 of the 431 eligible lung cancer cases. Two surgical pathologists from the Department of Pathology at the University of Iowa Hospitals and Clinics reviewed the pathology material. The major diagnostic groups were based on the World Health Organization's histologic typing of lung tumors and included the major categories of small cell carcinoma, squamous cell carcinoma, adenocarcinoma, and large cell carcinoma [17]. The reviewers were blinded to the diagnosis on the pathology report as well as to each other's review diagnosis. When the designated histologic type of tumor differed between the two reviewers, they reviewed the pathologic material simultaneously and rendered a consensus diagnosis. To ensure comparability of data, criteria for diagnosis were made based on light microscopic observations. In some cases, special stains such as mucicarmine, PAS, or PAS after diastase were requested on the tissue blocks by the reviewing pathologists to arrive at a reliable diagnosis. Three hundred sixty lung cancer cases (84%) were included in the analysis after 71 cases were deleted for either not completing the dietary questionnaire or failing the food-frequency questionnaire edit (see food frequency questionnaire).

2.2. Control participants

A population-based sample of controls was ascertained by two methods. The Iowa Department of Transportation provided a random sample of state drivers license files for women age 40–64. Among women ages 65–84 years, controls were generated from the Health Care Finance Administration's (HCFA) roster of Medicare recipients, which includes an estimated 95% of women in this age group. If a selected control had a diagnosis of a primary invasive lung cancer at the time of initial contact, she was excluded. Before contacting each HCFA control, a letter provided by the Department of Health and Human Services describing the study and the study participants rights was sent as mandated by the HCFA. The control group was age-frequency matched to the case series by 5-year age groups. A control contact letter, which described the study, was sent to the potential participant followed by a telephone call to assess eligibility and to obtain her consent for participation in the study.

Forty-eight percent of the controls lived in their current home for at least 20 years. One thousand three hundred thirty-seven eligible controls were identified between May 1, 1993 and October 30, 1996. Six hundred and ninety-three of the controls (52%) consented to take part in the study and 574 (83%) correctly completed the detailed dietary questionnaire. One hundred and nineteen controls were deleted for either not completing the dietary questionnaire or failing the food-frequency questionnaire edit (see food frequency questionnaire).

A follow-up questionnaire that compared smoking and working histories was routinely sent to eligible controls who refused to participate in the study. Two hundred and twenty-four controls returned their questionnaire (36% of non-participating controls). Comparisons were made between participating and non-participating controls based on the questionnaire responses to having ever worked outside the home, current working status, and smoking history. In addition, the eligible controls that returned the short questionnaire were offered year-long radon testing of their bedroom.

2.3. Food frequency questionnaire

A modified version of the 60-item NCI-Block Food Frequency Questionnaire (FFQ) (i.e. a 70-item food frequency questionnaire) was used to obtain information on usual diet (frequency of consumption) approximately 2–3 years before study enrollment [18]. The 70-item questionnaire used in this study did not include portion size, but was modified to more accurately assess fat intake and to provide more detailed assessment of vegetables consumed. The dietary questionnaire was processed using the NCI-Block analysis program for personal computers [18]. Both the food list and the nutrient values associated with each line item were developed with dietary data obtained from adult respondents to the Second National Health and Nutrition Examination Survey [18]. The FFQ were edited according to standard criteria [18] to identify and remove individuals whose diet records yielded extremely low (i.e. less than three food items per day) or high scores (i.e. 30 food items per day) for total amount of food consumed, or who skipped too many food items (i.e. more than 15%).

2.4. Analysis

Odds ratios (OR) and 95% confidence intervals (CI) were calculated using multiple logistic regression [19]. We initially examined numerous potential confounding factors, including age, pack–years of smoking, yellow–green vegetable intake, fruit and fruit juice intake, nutrient density calories, body-mass-index (BMI) and alcohol consumption, as continuous variables. While previous non-malignant lung disease (yes, no), number of years of education completed (<12, ≥ 12 years) were examined as dichotomous variables. We evaluated trend in the logistic regression analyses by converting the ordinal exposure variable to a categorical variable, which then was treated as continuous by coding it as 1, 2, 3, 4, 5. Trend tests based on median quintile values gave similar results.

The nutrient density approach was used to examine the effect of dietary constituents [20]. The nutrient density coefficient for total fat intake for

example, represents the effect of increasing the percentage of fat (or any other macro nutrient) in the diet while keeping total energy intake constant [21].

3. Results

The mean age of the 360 case participants and the 574 control participants was 67 years. Controls differed from cases in a number of socio-demographic characteristics. Controls had a significantly greater proportion of participants with post-high school educations (44.6 vs. 32.8%, respectively). Far fewer controls were current smokers (7.8%) and former smokers (25.1%) than cases (23.9% current smokers and 60.3% former smokers). Previous non-malignant lung disease occurred in 25.1% of controls but in 43.6% of cases. Only 9.6% of controls were in the highest quartile of alcohol consumption, while 20.3% of the cases were in the highest quartiles of alcohol consumption. Thirty-eight percent of cases were in the two highest BMI quartiles vs. 47% of the controls (Table 1).

Age and nutrient density calorie adjustment were performed for all analyses in Table 2. Significant linear trends in lung cancer risk were observed with an increase in total fat, saturated fat and cholesterol consumption. A significant decrease in lung cancer risk was observed with an increase in carbohydrate consumption and protein consumption (Table 2). A significant trend in lung cancer risk was also observed with increasing total meat consumption ($P = 0.025$). However, when we partitioned total meat consumption into red meat and white meat, we found an excess lung cancer risk associated with red meat consumption and a decreasing risk with increasing white meat consumption. Dairy products did not influence lung cancer risk among Iowa women. Yellow–green vegetables and fruit/fruit juices intake were associated with a significantly diminished risk in this population.

The increased lung cancer risk with red meat consumption persisted (OR = 3.3; 1.7–7.6 comparing the highest to the lowest quintile) when we added saturated fat and cholesterol intake to the model (Table 3) along with age, education, pack–years of smoking, yellow–green vegetable intake, fruit/fruit juice intake, nutrient density calories, previous lung disease, alcohol consumption and

Table 1
Socio-demographic characteristics of case subjects and control subjects

Characteristics	Case subjects (%)	Control subjects (%)
Total	360	574
Age at interview, years		
<55	36 (10.0)	47 (8.2)
55–64	102 (28.3)	176 (30.6)
65–74	148 (41.1)	238 (41.5)
75–79	45 (12.5)	71 (12.4)
>79	29 (8.1)	42 (7.3)
Mean Age	66.98	66.76
Education, years		
<12	40 (11.1)	43 (7.5)
12	202 (56.1)	275 (47.9)
>12	118 (32.8)	256 (44.6)
Smoking history		
Never	57 (15.8)	385 (67.1)
Former	217 (60.3)	144 (25.1)
Current	86 (23.9)	45 (7.8)
Histologic type		
Adenocarcinoma	139 (38.6)	NA
Squamous cell	64 (17.8)	NA
Small cell	63 (17.5)	NA
Other cell type	66 (18.3)	NA
Missing cell type[a]	28 (7.8)	NA
Previous lung disease		
No	202 (56.1)	430 (74.9)
Yes	157 (43.6)	144 (25.1)
Missing	1 (0.3)	0
Alcohol consumption (drinks/week)		
1 (0)	227 (63.1)	401 (69.9)
2 (>0–0.7)	25 (6.9)	61 (10.6)
3 (0.71–4.2)	35 (9.7)	57 (9.9)
4 (>4.2)	73 (20.3)	55 (9.6)
Body mass index		
1 (<21.9)	110 (30.6)	144 (25.1)
2 (21.9–24.0)	93 (25.8)	135 (23.5)
3 (24.1–26.6)	60 (16.7)	135 (23.5)
4 (>26.6)	77 (21.4)	135 (23.5)
Missing	20 (5.5)	25 (4.4)

[a] Individual diagnosis slides were not available for consensus review.

Table 2
Odds ratios[a] for macro-nutrients and selected food groups

Diet factor	Quintiles of consumption					*P* value for trend
	1 (lowest)	2	3	4	5 (highest)	
Carbohydrate	1.0	0.4 (0.3–0.6)	0.6 (0.4–0.9)	0.3 (0.2–0.5)	0.3 (0.2–0.4)	<0.001
Protein	1.0	0.8 (0.5–1.3)	0.9 (0.6–1.3)	0.7 (0.4–0.99)	0.6 (0.4–0.9)	0.012
Fat	1.0	1.1 (0.7–1.8)	1.6(1.0–2.5)	1.9 (1.2–2.9)	2.0 (1.3–3.1)	<0.001
Saturated fat	1.0	0.94 (0.6–1.6)	1.8 (1.1–2.8)	1.9 (1.2–3.1)	3.0 (1.9–4.7)	<0.001
Cholesterol	1.0	1.1 (0.7–1.8)	1.0 (0.6–1.6)	1.7 (1.1–2.6)	2.0 (1.3–3.0)	<0.001
Meat	1.0	1.2 (0.7–1.94)	1.3 (0.8–2.0)	1.3 (0.8–2.0)	1.8 (1.1–3.0)	0.025
Red meat	1.0	1.3 (0.8–2.1)	1.6 (1.0–2.6)	2.0 (1.2–3.4)	2.7 (1.6–4.5)	<0.001
Chicken & fish	1.0	1.1 (0.7–1.6)	0.7 (0.5–1.2)	0.9 (0.6–1.3)	0.6 (0.4–0.94)	0.016
Dairy	1.0	0.8 (0.5–1.2)	0.7 (0.4–1.0)	0.8 (0.5–1.3)	0.9 (0.6–1.4)	0.600
Yellow–green vegetables	1.0	0.6 (0.3–0.8)	0.6 (0.4–0.9)	0.4 (0.2–0.6)	0.3 (0.2–0.6)	<0.001
Fruit–fruit juices	1.0	0.6 (0.4–0.8)	0.6 (0.4–0.92)	0.4 (0.3–0.6)	0.4 (0.3–0.6)	<0.001

[a] Odds ratios adjusted for age and nutrient density calories.

BMI. The significant linear trend for the two macro nutrients in the model (saturated fat highest vs. lowest quintile OR = 1.2; 0.6–2.3 and cholesterol OR = 1.1; 0.6–2.0) disappeared. The excess risk for alcohol consumption (highest vs. lowest quartile OR = 1.5; 0.93–2.5) and BMI (highest vs. lowest quartile OR = 1.1; 0.7–1.5) disappeared in this full adjusted model (not shown in table) as did the protective effects of fruits/fruit juices (highest vs. lowest quintiles OR = 1.4; 0.7–0.8–2.5), carbohydrate intake (highest vs. lowest quintiles OR = 1.0; 0.7–1.4) and protein intake (highest vs. lowest quintiles OR = 1.0; 0.7–1.4).

When we substituted white meat for red meat in the complete model described above, white meat was not associated with a significant excess risk of lung cancer (the odds ratios for quintiles 1–5 were 1.0 [reference group], 1.4, 1.1, 1.6, 1.4 [*P* for trend = 0.49], respectively, data not shown in table). To evaluate for potential effects modification between smoking and red meat consumption and between lung cancer cell type and red meat consumption, we performed the analysis described for Table 3 after stratifying by smoking history and cell type (Table 4). Stratification reduced statistical power, but no significant differences were seen between the two smoking strata or between the two cell type strata. Among the combined group of never smokers and former smokers, when we compared the highest to the lowest quintile of consumption we observed an odds ratio 2.8 (1.4–5.4), while among current smokers we observed an odds ratio of 4.9 (1.1–22.3). For study participants with adenocarcinoma we observed an odds ratio of 3.0 (1.1–7.9). Among cases with non-adenocarcinoma we observed an odds ratio of 3.2 (1.3–8.3). In a supplemental analysis shown in Table 5, we partitioned red meat consumption into meats cooked at high temperature versus meats cooked at lower temperatures, adjusting for all the variables previously used in the model described for Table 3. Red meat cooked at 'high temperatures' included meat that was pan fried, deep fried, roasted or grilled, while meat that was 'cooked at low temperature' include meat such as frankfurter (hot dogs) that were boiled, or the meat of meat pies that were baked in a semi-liquid meat gravy within a pie crust or meat prepared in the tomato/meat sauce of spaghetti. The observed odds ratio for both groups were elevated and indistinguishable in these data. The odds ratio for the fifth compared to the first quintile of meat intake was 2.3 (1.7–7.6) for red meats cooked at high temperatures and 2.0 (1.1–3.5) for red meats cooked at lower temperatures.

Data from the follow-up questionnaire found no difference between participating and control refusals for the categories: ever-worked, current worker, ever smoked, current smoker. In addition, no significant differences were noted in the bedroom radon concentrations (Wilcoxon rank-Sum Test, $P = 0.17$) between participating controls and the control refusals (21%), who performed radon testing.

4. Discussion

In several previous studies total fat, saturated fat and/or cholesterol were associated with increased risk of lung cancer [1–6], as they were in univariate analysis among Iowa women studied here. Among Iowa women, lung cancer risk was higher for those participants who were frequent meat consumers and this excess risk persisted after adjusting for the effect of total fat, saturated fat and cholesterol, smoking and yellow–green vegetable consumption. Neither fat, saturated fat, nor cholesterol remained significant after adjusting for the effect of meat consumption. When we differentiated between red meat and white meat, all of the excess lung cancer risk was associated with red meat consumption only. While limited sample size prevented us from examining this relationship for each individual lung cancer cell type, both adenocarcinoma and non-adenocarcinoma study participants were at similar excess risk from red meat consumption. Similar lung cancer risks were observed for current smokers and the combined group of ex-smokers and lifetime nonsmokers, mitigating the possibility that lingering uncontrolled confounding from cigarette smoking was responsible for the red meat effect found here.

Table 3
Odds ratios[a] for quintiles of indicated food items

Diet	Odds ratio	95% CI	*P* value for linear trend
Red meat (times/week)			
<3.5	1.0 (ref.)		
3.5–5.5	1.7	(0.9–3.3)	
5.6–7.6	2.0	(1.4–4.0)	
7.7–9.8	2.5	(1.2–5.2)	
>9.8	3.3	(1.7–7.6)	0.005
Saturated fat (g/day)			
<14.2	1.0 (ref.)		
14.2–19.0	0.6	(0.3–1.1)	
19.1–24.8	1.1	(0.6–2.1)	
24.9–33.0	1.0	(0.6–2.0)	
>33.0	1.2	(0.6–2.3)	0.259
Cholesterol (mg/day)			
<124.5	1.0	(0.4–1.3)	
124.5–166.7	0.7	(0.3–1.2)	
166.8–219.9	0.6	(0.3–1.2)	
220.0–301.4	1.2	(0.6–2.2)	
>301.4	1.1	(0.6–2.0)	0.210
Yellow–green vegetables (times/week)			
<0.7	1.0		
0.7–<1.4	0.5	(0.3–0.8)	
1.4–<2.1	0.6	(0.4–1.1)	
2.1–<2.8	0.5	(0.2–0.7)	
≥2.8	0.4	(0.2–0.7)	0.018

[a] Adjusted for age, education (<12, 12, >12), pack–years, smoking history (current, former, never), fruits/fruit juices intake, nutrient-density calories, previous lung disease (yes vs. no), alcohol consumption (quartiles) and BMI.

In an earlier study, the excess risk of lung cancer associated with red meat consumption disappeared when data from proxy respondents were removed [22]. That was not the case in this study where 70% of the participating cases were alive at interview. Meat cooked at high temperatures produces various pyrolysis products depending on the cooking methods used. A family of compounds known as heterocyclic amines (HCA) is produced when meats are cooked at high temperature, particularly pan-frying and grilling/barbecuing [23–25]. HCAs are formed when creatine and amino acids in meat juices pyrolyze. These compounds are highly mutagenic in Ames Salmonella tests, and are carcinogenic in animal studies. Since heterocyclic amines found in cooked red meat [10,25] may increase lung cancer risk, we stratified red meat consumption into red meat cooked at high temperatures vs. red meat cooked at lower temperatures and found no significant difference in risk between the cooking strata. While this finding provides no support for the heterocyclic amine hypothesis, the absences of questions on cooking practice and doneness levels leave open the possibility that well done red meats may be responsible for some portion of the excess risk observed.

Table 4
Odds ratios[a] for red meat consumption by smoking history and cell type

Characteristic	Odds ratio'(for 5th [highest] vs. 1st [lowest] quintile of red meat consumption among controls)	95% Confidence interval
Smoking history		
Never smokers-former smoker	2.8	(1.4–5.4)
Current smokers	4.9	(1.1–22.3)
Cell type		
Adenocarcinoma	3.0	(1.1–7.9)
Non-adenocarcinoma	3.2	(1.3–8.3)

[a] Adjusted for age, education (<12, ≥12), pack–years (<12, 12, >12), smoking history, green–yellow vegetables intake, fruits/fruit juices intake, nutrient-density calories, previous lung disease (yes vs. no), alcohol consumption (quartiles) and BMI.

Dairy products were not observed to influence the risk of lung cancer among Iowa women. Previous studies have shown varied results with some showing dairy products to be a lung cancer risk factor [7,26–30], with others showing dairy products to be protective [9,30] and yet others showing dairy products to have no effect on lung cancer risk [31–35]. The varying nutrient content of dairy products may explain the varying effect on lung risk in different studies. The fat intake from whole milk and other dairy products, for example, has been hypothesized to be responsible for the excess lung cancer risk observed in a study from Sweden [7] where dairy products are an important source of fat in the diet. In Sweden a significant excess risk of lung cancer was observed among women and men who consumed milk 'several times/day' [7], but no significant excess lung cancer risk was seen among women from Missouri or women from this study (Iowa) where women in the highest milk intake categories consumed greater than 16.8 and 19.6 servings of milk per week respectively (not shown in table). It is likely that the mechanism by which milk and other dairy product influence lung cancer risk, if any, is not simple. Milk is a complex mixture of fat, protein, preformed vitamin A (retinol), calcium and vitamins and the varying concentrations of these nutrients in different areas could account for the confusing picture seen to date.

Vegetables, particularly yellow–green vegetables, were associated with a reduced risk of lung cancer and this protective effect was not influenced by red meat consumption, smoking nor any other risk factor observed in this study. Some, but not all cohort studies and the majority of case-control studies have reported significant protective effects of fruits and vegetable intake [36–38] on lung cancer risk. Fruits/fruit juices were not found to be protective of lung cancer if simultaneously adjusted for red meat and yellow–green vegetables. Other factors including alcohol, BMI, carbohydrate intake and protein intake which were shown to elevate or diminish risk in the age and calorie adjusted model, were no longer significant in the fully adjusted model. Few previous studies have had the capability to simultaneous

Table 5
Odds ratios[a] for red meat consumption by cooking temperature

Quintiles	Odds ratios (95% CI)	
	Red meat, high temperature cooking	Red meat, lower temperature cooking
1	1.0	1.0
2	1.7 (0.89–3.11)	1.3 (0.72–2.39)
3	1.2 (0.65–2.34)	2.2 (1.19–4.02)
4	2.0 (0.99–4.21)	2.3 (1.28–3.99)
5	2.9 (1.44–5.71)	2.1 (1.17–2.39)
	P for trend = 0.01	P for trend = 0.04

[a] Adjusted for age, education (<12, ≥12), pack–years, smoking history, green–yellow vegetable intake, fruits/fruit juices intake, nutrient-density calories, previous lung disease (yes vs. no), alcohol consumption (quartiles) and BMI.

adjust risk estimates by all of these dietary and anthropomorphic factors, and our results for both vegetables and fruits/fruit juices are consistent with the literature prior to use of the fully adjusted model [36–38].

A strength of this study was the rapid-reporting procedure employed which obtained a high percent of live cases. The use of living participants provides the best opportunity to obtain valid food frequency estimates. A limitation of this study was the lower than expected response rates for controls, which is partially attributable to the inclusion criterion of a 20-year residency in the current home. Although it is possible that a bias may result from including a disproportionate number of health conscious controls compared to cases, the fact that the excess risk of lung cancer was not significantly different between current smokers and the group of combined ex-smokers and former smokers mitigated the possibility that our observations are due solely to such a bias. Moreover, the follow-up questionnaire findings support the representativeness of the participating controls. Another limitation of the study was that dietary polycyclic aromatic hydrocarbons, a by-product of grilling, could also be a lung carcinogen and we could not assess this hypothesis since we did not have detailed questions on meat-cooking techniques. However, since only a small portion of meals in Iowa are typically grilled this is unlikely to be a major source of bias in this study.

In summary, this study provides additional support to the hypothesis that the consumption of red, but not white, meat is associated with an excess risk of lung cancer. This risk was independent of the smoking history, fruit consumption, yellow–green vegetable consumption, or the fat content of the diet. Furthermore, no significant effect modification was seen for smoking or cell type as these relate to red meat consumption. Since information concerning cooking practices was not collected in the investigation, we cannot address whether heterocyclic amines found as pyrolysis products of cooked meats played a role in the excess lung cancer risk observed. Since an excess risk was observed in both red meats cooked at high temperatures and at lower temperatures, our results suggest that heterocyclic amines may only partial account for the excess risk observed. Although diets low in vegetables and high in red meat intake may contribute to the overall risk of lung cancer, the single greatest reduction in lung cancer risk would be achieved by smoking cessation.

Appendix A. Food groups (see Ref. [18])

Fruit and fruit juice
- Apples and apple sauce, pears
- Cantaloupe (in season)
- Oranges, tangerines
- Oranges juice, grapefruit juice
- Grapefruit
- Koolaide or fruit drinks with vitamin C

Yellow–green vegetables
- Broccoli
- Spinach (cooked)
- Collards, kale, greens
- Carrots, mixed vegetables with carrots
- Sweet potatoes

Red meat

Cooked-high temperature	Cooked-lower temperature
Hamburger, beef burritos, meatloaf	Beef stew, pot pie
Beef (fat unspecified)	Spaghetti
Pork (fat unspecified)	Ham, lunch meats
Bacon	Liver
Sausage	Hot dogs

White meat (chicken and fish)
- Fried chicken (fat unspecified)
- Other chicken (fat unspecified)
- Fried fish
- Fish broiled or baked

Dairy
- Butter
- Ice cream
- Cheese and cheese spread
- Flavored yoghurt, frozen yoghurt

Whole milk (beverage)
2% Milk
Skim milk
Milk in coffee/tea

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